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SUMMARY

This was a directed inspection conducted under CP 7356.002 "DRUG MANUFACTURING INSPECTIONS" in response to District notification from this firm of a recall situation involving five lots of Children's OTC cough/cold medications possibly packaged with a dosing cup not containing the ½ teaspoon dosing mark for children ages 2-6. Products involved included:

1) Children's Mucus Relief, Grape Flavor, Expectorant/Guaifenesin (Lot (b) (4)
2) Children's Mucus Relief, Cough, Cherry Flavor, Dextromethorphan HBr/Guaifenesin (Lots (b) (4) (b) (4)
3) Tussin DM Cough Suppressant Expectorant for Children & Adults (Lot (b) (4)
4) Tussin DM cough Sugar Free Cough Suppressant Expectorant; Dextromethorphan HBr/Guaifenesin (Lot (b) (4)

The initial district notification and health hazard supplied indicated these lots had been shipped but remained under control in customer warehouses (see EF for email dated 8/31/07 from Shawn Shirazi to Sandra L. Williams).

In addition, information requested by CDER's Office of Compliance (see EF for email dated 9/4/07 from Kevin Budich) regarding 5 (b) (4) and 3 (b) (4) lots of children's OTC products, not associated with the recalls, were also collected and attached to this report.

Inspectional findings include: packaging materials are not representatively sampled and examined upon receipt and before use in packaging of a drug product; and SOPs associated with sampling of packaging materials not followed. Management promised a written response.

ADMINISTRATIVE DATA

Inspected firm:	L. Perrigo Co.
Location:	515 Eastern Ave Allegan, MI 49010-9070
Phone:	269-827-2296
FAX:	
Mailing address:	515 Eastern Avenue Allegan, MI 49010
Dates of inspection:	9/5/2007, 9/6/2007, 9/7/2007, 9/13/2007
Days in the facility:	4
Participants:	Patsy J Domingo, Investigator

HISTORY

For firm's inspection history see EIR dated 11/7-12/15/06.

FMD-145

Send any correspondence to:
Joseph C. Papa, President ,Chief Executive Officer
L. Perrigo Co.
515 Eastern Avenue
Allegan, Mi 49010

INTERSTATE COMMERCE

Interstate commerce was documented as physical samples of (b) (4) lots shipped were collected. A physical sample of the (b) (4) lot was not available as the entire lot had been shipped to the customer. In addition, packaging and distribution records were collected for the portion of each of the (b) (4) lots released as follows:

Lot (b) (4) Children's Mucus Relief, Grape Flavor, Expectorant/Guaifenesin

Exhibit 441 is the listing of production orders packaged under lot ((b) (4) A total of (b) (4) different customer labels were utilized for a total of (b) (4) bottles. Distribution documentation was collected for those bottles labeled under the (b) (4) label (material number (b) (4)) as a portion of this lot was shipped and is subject of this recent recall. A total of (b) (4) bottles were labeled under this Major label as documented in the packaging batch record attached as **Exhibits 442/446**. A total of (b) (4) bottles labeled were shipped to (b) (4) location as documented in the Sold-To/Ship-To Detail Report (**Exhibits 447**) and were shipped (as documented on Straight Bill of Lading) via (b) (4) on 8/16/07 (**Exhibit 448**). A second shipment of (b) (4) bottles was shipped to (b) (4) location as documented in the Sold-To/Ship-To Detail Reports (**Exhibits 449**) and were shipped and via (b) (4) (**Exhibit 450**) on 8/15/07. A physical sample (b) (4) bottle) of this lot was collected. In addition (b) (4) physical samples of this lot were packaged by and shipped by Perrigo to CDER's Office of Compliance.

Copies of the other (b) (4) packaging records for label brands (b) (4) were also collected and are attached as **Exhibits 451/476**.

Lo (b) (4) Children's Mucus Relief, Cough, Cherry Flavor, Dextromethorphan HBr/Guaifenesin

Exhibit **477** is the listing of production orders packaged under lot # (b) (4) A total of (b) (4) different customer labels were utilized for a total of (b) (4)) bottles. Distribution documentation was collected for those bottles labeled under the (b) (4) labels (material numbe (b) (4)) as a portion of each of these were shipped and subject of this recent recall. A total of (b) (4)) bottles were labeled under the (b) (4) label as documented in the packaging batch record attached as **Exhibits 478/482**. Of those labeled (b) (4) bottles were shipped to (b) (4) located in (b) (4) as documented in the

Sold-To/Ship-To Detail Report (**Exhibit 483**) and bill of lading (**Exhibits 484/485**) dated 8/17/07. An additional (b) (4) bottles were shipped to (b) (4) location as documented in Sold-To/Ship-To Detail Report (**Exhibit 486**) and bill of lading (**Exhibits 487**) dated 8/16/07.

A total of (b) (4)) bottles were labeled under the (b) (4) label as documented in the packaging batch record attached as **Exhibits 488/492**. Of those labeled, (b) (4) bottles were shipped to (b) (4) location (see **Exhibits 493/494**) and (b) (4) bottles were shipped to (b) (4) facility (see **Exhibits 495/496**).

(b) (4)) bottles were labeled under the (b) (4) label as documented in the packaging batch record attached as **Exhibits 517/521**. Of those labeled, (b) (4) bottles were shipped to (b) (4) as documented in **Exhibits 522/523**.

The remaining portions of lot (b) (4) were labeled under (b) (4) (**Exhibits 497/501**), (b) (4) (**Exhibits 502/506**), (b) (4) (**Exhibits 508/511**), and (b) (4) (**Exhibits 512/516**) labels but not distributed. (b) (4)) of this lot was collected. In addition (b) (4) physical samples of this lot were packaged by and shipped by Perrigo to CDER's Office of Compliance.

Lot (b) (4) Children's Mucus Relief, Cough, Cherry Flavor, Dextromethorphan HBr/Guaifenesin

Documents entitled "Batch Summary" and "Production Orders by Batch" attached as **Exhibits 524/525** document that this lot had been labeled under just the one label belonging to Rite Aid (Material Number (b) (4)). A total of (b) (4)) bottles were finish packaged as documented in Customer Packaging Order attached as **Exhibits 526/530**. The entire quantity packaged was shipped out to two (b) (4) locations as follows: (b) (4) bottles were shipped to the (b) (4) distribution center as documented in **Exhibits 531/532** on 8/17/07; and the remaining (b) (4) bottles were shipped to (b) (4) Customer Support Center located in (b) (4) as documented in **Exhibits 533/534**. I did not collect a physical sample of this, however, Perrigo did shipped a bottle from their reserve sample to CDER's Office of Compliance.

Lot (b) (4) Tussin DM Cough Suppressant Expectorant for Children & Adults

Documents entitled "Batch Summary" and "Production Orders by Batch" attached as **Exhibits 535/536** document that (b) (4) different customer labels were utilized for a total of (b) (4)) bottles. Distribution documentation was collected for those bottles labeled under the (b) (4) label (material number (b) (4) as the entire quantity of this lot was shipped and is subject of this recent recall. A total of (b) (4) bottles were finish packaged under the (b) (4) label as documented in the Customer Packaging Order batch record attached as **Exhibits 557/561**. All (b) (4) bottles were shipped to (b) (4) on 8/15/07 as documented by Sold-To/Ship-TO Detail Report (**Exhibit 562**) and Straight Bill of Lading (b) (4) (**Exhibit 563/564**).

The remaining portions of lot (b) (4) were labeled under (b) (4) (**Exhibits 537/541**), (b) (4) (**Exhibits 542/546**), (b) (4) (**Exhibits 547/551**), (b) (4) (**Exhibits 552/556**), (b) (4) (**Exhibits 565/569**) and (b) (4) (**Exhibits 570/574**) labels but were not distributed. A sample of this lot, packaged under the (b) (4) label, was collected by me and Perrigo shipped (b) (4) physical samples to CDER's Office of Compliance as well.

Lo(b) (4) Tussin DM cough Sugar Free Cough Suppressant Expectorant; Dextromethorphan HBr/Guaifenesin

Documents entitled "Batch Summary" and "Production Orders by Batch" attached as **Exhibits 575/576** document that (b)(4) different customer labels were utilized for a total of (b) (4)) bottles. Distribution documentation was collected for those bottles labeled under the (b) (4) label for customer (b) (4) (material number (b) (4)) as a portion of this lot was shipped and is subject of this recent recall. A total of (b) (4) dozen bottles were labeled under the (b) (4) label as documented in the Customer Packaging Order batch record attached as **Exhibits 582/586**. A portion of those bottles were shipped to each of (b)(4) differen (b) (4) facilities located in (b) (4) . The Sold-To/Ship-To Detail Report and corresponding Bill of Lading are attached as **Exhibits 587/628**. The remaining portions of lot (b) (4) were labeled under (b) (4) (**Exhibits 577/581**), (b) (4) (**Exhibits 629/633**), (b)(4) (**Exhibits 634/638**), and (b) (4) (**Exhibits 639/643**) labels but were not distributed. A physical sample (b) (4) of this lot was collected. In addition (b)(4) physical samples of this lot were packaged by and shipped by Perrigo to CDER's Office of Compliance.

JURISDICTION

See Interstate Commerce section above.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

Credentials were shown and FDA-482, Notice of Inspection was issued to Rene Robbins, Director Quality Assurance Tablet Value Stream. Ms. Robbins, and Tami Frederick, Director of Quality Liquid Value Stream were responsible for requesting documents, answering questions and arranging for the subject specialists to answer questions I had.

Other individuals who took part in this inspection include:
Louis W. Yu, Ph.D., Sr. VP Global Quality and Compliance
Paul Weninger, VP CHC Global Quality Operations
Shawn Shirazi, Ph.D., Sr. Director Pre-Commercial Quality & Technology
John D. Brown, QA External Operations Director
Kareena Parris, QA Manager

At the conclusion of this inspection, FDA-483, Inspectional Observations was issued to Louis W. Yu as I was told he would be the most responsible available at that time. However, Joseph C. Papa, President Chief Executive Officer was also present for this meeting.

Dr. Yu was the main spokesperson regarding any discussions about the recall. He and Dr. Shirazi participating in discussions regarding the recall and CDER's request, relayed via telephone by Compliance Officer Sandra Williams from the Detroit District Office for samples of product involved in the recall and samples of all products packaged with dosing devices.

With regard to the remainder of the affected lots not distributed, Dr. Yu indicated they would have to determine whether the lots would be reworked for distribution or rejected. This decision had not been made prior to the conclusion of this inspection.

FIRM'S TRAINING PROGRAM

Not covered

MANUFACTURING/DESIGN OPERATIONS

Purchased Dosing Cups

Reportedly there is no written agreement between Perrigo and manufacturer of the dosing cups (b) (4) This cup supplier location was just recently, 4/2007, approved as a supplier of plastic dosing cups. Perrigo has utilized (b) (4) as their cup manufacturer since at least March 1998 but this (b) (4) location is a new (b) (4) location and therefore new to Perrigo as well.

When I requested documentation regarding the qualification of (b) (4) (b) (4) I was provided the document entitled (b) (4) (**Exhibits 57/59**). This document lists the date qualified as 4/12/07. This document prepared by (b) (4) XP, contains instructions: "(b) (4) t."

Events that lead to the recall are as follows:

There had been a request by Perrigo engineering group to produce a number of slightly larger cups to use in the R & D process to facilitate a future change to a larger bottle cap on the drug product containers. (b) (4) the cup manufacturer, had chosen to substitute 5 of the approved cup cavities with 5 experimental, larger, cup cavities in order to fill this request, and choose to run this as part of production lot (b) (4). The experimental cups were contained to the West production line, and were to be run through the West production line rim roller, boxed and set aside. The experimental cups were to be pulled from the line as they were made, ran through the rim roller and immediately placed into a box for Perrigo engineering.

As described in Perrigo's DMAIC Deviation Document (b) (4) (**Exhibits 331/341**) "(b) (4) ." Regulatory Affairs and the cup manufacturer (b) (4) were notified and all affected material was placed on hold.

(b) (4) had initiated an investigation and a copy of that draft document is attached as **Exhibits 60/62**. A copy of (b) (4) "(b) (4) Rev. Level 2 dated 8/29/07 (**Exhibits 63/73**) was also provided as documentation of the quality checks (b) (4) performs routinely. This document includes pictures of the dose cup (side and bottom view); measurement equipment, packaging and labeling highlights. This quality check document states "a(b) (4)

According to (b) (4) investigation write-up a QA Auditor noticed an Inspector/Packer (temporary employee) was not following the special instructions given regarding the experimental cups and some of these experimental (bad) cups were allowed to be mixed with the rest of the (b) (4) production line cups. The line was shut down and an audit of the cases packed was performed. (b) (4) cases of cups were pulled from the production line and placed in the regrind room. The Inspector/Packers assured the QA Auditor that no other earlier product was mixed. The QA Auditor allowed the restart of the line. The QA Auditor also checked production prior to the incident and found no further issues.

Approximately (b) (4) hours into the run (end of a shift) the experimental cup cavities were pulled and replaced with the approved cup cavities and the line was to have been cleared of all the experimental cups produced. The batch continued to run for several more days (through 8/1/07) under batch (b) (4)

Reportedly there is no written agreement between Perrigo and this cup manufacturer regarding alerting Perrigo as to which production batch the ordered experimental cups were associated with, nor that there were problems associated with mixing the experimental (bad) and good cups during the production run.

Based on the way (b) (4) marks their cases, they were able to identify which shipments to Perrigo contained cases of Cups produced on 7/24/07. As can be seen on the time line prepared (**Exhibit 78**), Perrigo assigned receiving numbers (b) (4) each contained cups produced on 7/24/07. Lots produced using these two cup lot/receiving numbers were included in the recall.

Although the "Bad" cups were confined to boxes produced on the (b) (4)" production line during a (b) (4) time slot and cases are labeled to reflect this very line/date/time information, Perrigo does not record this information in their batch record. Only the incoming lot number assigned to the component is recorded in the batch record. Therefore, the recall had to include all lots packaged with cups from the (b) (4) receipts associated with the production date 7/24/07.

Dosing Cup History

Dosing Cup (b) (4) contained dosing lines representing ½ teaspoon up through 4 teaspoons. The ½ teaspoon mark was located in the bottom ring of the cup. See **Exhibit 1** for a diagram of this cup. Cup (b) (4) drawing bears an effective date of March 26, 1998. Cup # (b) (4) did not contain both teaspoon (tsp) and tablespoon (tbsp) dose lines. Reportedly this cup was the predecessor to dosing cup (b) (4) currently in use.

Dosing Cup (b) (4) which contains dosing lines representing ½ teaspoon up through 4 teaspoons. The ½ teaspoon mark is located in the bottom ring of the cup. This cup also contains a 1 TBSP dosing mark. Cup (b) (4) drawing bears an effective date of 10/26/00 (**Exhibit 2**), however the specification document (**Exhibits 3-4**) was not effective until 12/27/00.

Perrigo prepared Protocol 01-2006 entitled "Dosage Cup Volume Verification Test Procedure Using Distilled Water" (**Exhibit 79/82**) and the volume verification testing of Dosage Cup (b) (4) as well as Dosage Cup numbers (b) (4) was accomplished 3/27-28/06 (**Exhibits 83/92**).

The following is a list of products that reference the ½ tsp dose for children ages 2-6 years of age on the label and are packaged with Dosing Cup # (b) (4) (**Exhibit 329/330**):

Name/Product Number
Guaifenesin Grape Liquid ((b) (4))
Tussin MS Liquid ((b) (4))
Tussin CS Liquid ((b) (4))
Tussin DM Liquid ((b) (4))
Guaifenesin DM Cherry Liquid ((b) (4))
Phenylephrine Tussin CF Liquid ((b) (4))
Tussin DM Clear Liquid ((b) (4)

A document entitled "Customer Who Purchase Specific Formulas" (**Exhibit 95/98**) gives a listing of the different label brands each of the above listed products are packaged under. A more detailed document entitled "Customers and Sold-to's for cup (b) (4) for Formula's with ½ tsp dosage" (**Exhibits 99/110**) further identifies those customers listed in **Exhibits 95/98**.

In addition to the above, the following is a listing of products that do not reference the ½ tsp on the label (the lowest recommended dose being 1 tsp), that are packaged with Dosing Cup # (b) (4) (**Exhibit 93/94**):

Name	Product (formula) Number	Example Label Exhibit #
Bubble Gum APAP Susp	(b) (4)	(b) (4)
Grape Acetaminophen Susp	(b) (4)	(b) (4)
Ibuprofen Childrens Bubble Gum	(b) (4)	
Child's Non-Aspirin Susp Liquid	(b) (4)	
Loperamide	(b) (4)	
PE Triacting CC Daytime	(b) (4)	
IBUP SUSP Fruit	(b) (4)	
Ibuprofen 100 mg Children's Grape	(b) (4)	
Triacting Free Nitetime Grape	(b) (4)	
Ibuprofen 100 MG Children's Berry	(b) (4)	
Dibromm PE Grape Elixir	(b) (4)	
PE Triacting CC Nite	(b) (4)	

- Attached label examples contain a reference to ½ teaspoon ("80 mg per ½ teaspoon" in the net weight area of the label) although the lowest recommended dose is 1 teaspoon.

A printout was collected which lists all "Material Within Expiry Using Cup (b) (4) and is attached as **Exhibits 129/328**. This document lists all lots that have been produced/released to the marketed, using the (b) (4) cup, and are still in date

MANUFACTURING CODES

Not Covered

COMPLAINTS

Review of complaints was limited to complaints received regarding dosing cups. Attached as **Exhibit 6** is a listing of (b) (4) complaints received between the dates 1/1/2006 and 9/4/2007. Following is a summary of each of these complaints:

Complaint PCA (b) (4) (Perrigo Case #4753) (**Exhibits 7/14**)
Product Code (b) (4) Product Name: Tussin DM Lot (b) (4)
Complaint date: 2/17/06
Problem: The dosage cup is literally impossible to read. Suggested lines be printed in black.

Complaint (b) (4) (Perrigo Case (b) (4)) (**Exhibits 15/22**)
Product Code (b) (4) Product Name: Tussin DM Clear Lot #Unknown
Complaint date: 3/22/06
Problem: Dissatisfied with the cup. The medication is clear and so is the cup. The measurements on the cup are white/clear so you cannot see. Suggested measurement be printed in black ink rather than white.

Complaint (b) (4) (**Exhibits 23/31**)
Product Code (b) (4) Product Name: Ibuprofen 100 mg Child Berry Suspension Lot #Unknown
Complaint date: 8/3/06
Problem: Cup is marked in tbsp not tsp. She witnessed her husband almost giving the wrong dose. Possibility that the wrong cup was used by the consumer.

Complaint (b) (4) (**Exhibits 32/35**)
Product Code (b) (4) Product Name: Tussin DM Liquid Lot (b) (4)
Complaint date: 9/11/06
Problem: Parent exceeded the labeled dose for 8 year old child.

Complaint (b) (4) (**Exhibits 36/42**)
Product Code (b) (4) Product Name: Tussin DM Liquid Lot # Unknown
Complaint date: 9/26/06
Problem: Having a problem with the cup. Hard to see the dosage amounts

Complaint (b) (4)
Product Code (b) (4) Product Name: Tussin DM Liquid Lot (b) (4)
Complaint date: 10/24/06
Problem: "The little cup this comes with is not satisfactory"

Complaint # (b) (4)
Product Code (b) (4) Product Name: Tussin DM Clear Liquid Lot # Unknown
Complaint date: 5/18/07
Problem: The measurements are too difficult to see.

Complaint (b) (4)
Product Code (b) (4) Product Name: Tussin DM Liquid Lot (b) (4)
Complaint date: 11/20/06

Problem: "Consumer called to report that the dosage cup for the GE Tussin DM, identified by (b) (4), does not have the correct markings. The consumer states the markings are only in tablespoons when the dosing is in teaspoons". "The consumer thinks this could be very dangerous if someone doesn't pay attention. The consumer called back and reported that it does have teaspoon (TSP) and tablespoon (TBSP) labeled on the dosage cup but it is very confusing. She is not satisfied with the dosage cup labeling".

In each of these cases, the complaint was entered into the complaint database monitoring system ((b) (4)) for trending purposes, however, no investigation was initiated. This no investigation decision was based assessment there was no quality issue and is addressed in Perrigo Company SOP (b) (4)".

RECALL PROCEDURES

SOP (b) (4)" (Exhibits 644/663) was reviewed. No deficiencies were noted.

Upon arrival for this inspection, I was told all lots to be recalled had been placed on hold in Perrigo's warehouse. I was told by Dr. Yu that only a very small number of the defective cups were mixed into the lots produced and that they were awaiting CDER's input before the official recall would be sent out. They, Perrigo, felt this recall needed only be to the wholesale level. Dr. Yu further stated that based on previous experience, their customers would not place product on hold without an "official recall letter". Later that same day (after the lunch break) I was told that one customer, (b) (4) had agreed to hold product without the official letter. Upon further discussion at the end of the first day of inspection, I learned from Dr. Yu that the other (b) (4) customers had not been contacted and given the option of holding product prior to receiving the official recall letter.

Upon arrival the 2nd day I was told all customers had been notified both via telephone and by letter and that all customers had placed their inventory on hold. What was unknown was whether or not any of the lots had been released to the marketplace. Prior to the conclusion of this inspection it was verified that (b) (4) units had been released to the retail level and need to be recalled back.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

Observations listed on form FDA 483

OBSERVATION 1

Labeling and packaging materials are not representatively sampled and examined upon receipt and before use in packaging and labeling of a drug product.

In the case of liquid drug dosing cups, there are two equipment lines utilized in the production of a "batch" or run. Your sampling plan does not attempt representative sampling of these two production lines. Current sampling plan failed to detect the presence of experimental cups, lacking the 1/2 teaspoon dosing measure, found to be present in the portion of your supplier's batch (b) (4) received as Perrigo batch #'s (b) (4) . Examples: (b) (4) (b) (4) (b) (4) (b) (4) (b) (4)

Reference: 21 CFR 211.122(a)

Supporting Evidence and Relevance:

The dosing cup manufacturer, "(b) (4) XP" (aka Express Packaging Solutions) has a two sided line set up where dosing cup (b) (4) is produced. Attached as **Exhibit 74** is a diagram of the cup cavity set up on (b) (4) production line. Each of the (b) (4) cavities has a unique mold number which is embossed in the bottom of the finished cup. The line has a Plexiglas divider which separates the cups as they are fed to the two rim rolling lines which (b) (4) refers to as (b) (4) . In the picture the cavities are essentially numbered 1 through 110. There are five cup locations, (b) (4) that contain the numbers (b) (4) and are colored yellow in the diagram. These represent cavities that had to be replaced over time due to ware. In addition (b) (4) of the cup locations, (b) (4) are colored green. The green represents the experimental die cavities temporarily placed onto the line to produce the larger cups ordered by Perrigo R & D engineers. Once removed from the line the currently approved cavity mold numbers (b) (4) were to replace their experimental counterpart.

Once the manufacturing process is complete, cup numbers (b) (4)) are packaged into cases which are labeled such to identify them as having come off the (b) (4) portion of the production line. Likewise, cup numbers (b) (4)) are packaged into cases which are labeled identifying them as produced on the East production line.

The photographs found in **Exhibits 75-77** show what an individual cup cavity and corresponding cup bottom identification "insert" look like. The cavities pictured with the blue rim at the top are the experimental cavities. This coloring helped (b) (4) identify which were the experimental cup molds and their placement in the equipment set up. (b) (4) has (b) (4) such cavities that must be set up each time a batch of Cup (b) (4) is produced.

Perrigo has several SOP's associated with the inspection and sampling of incoming components: SOP (b) (4) " documents the procedures for the inspection of incoming shipments of various components including dosage cups, droppers, and syringes (**Exhibits 342/346**). This SOP refers to (b) (4) ((b) (4) for Delivery Devices.

Physical Defect Criteria (b) (4) (**Exhibits 347/348**) lists what the various defects (Critical, Major or Minor) might be. Included in the lists is critical defect "Illegible, incorrect, missing embossing" and major defect (b) (4) ".

SOP (b) (4) " (**Exhibits 349/355**). This SOP's sampling section refers to (b) (4) ".

SOP (b) (4) " (**Exhibits 356/362**) includes the two sided form, the back side of which includes a column for listing/recording the mold numbers inspected.

SOP (b) (4) " (**Exhibits 363/368**) describes Perrigo's three inspection plans (Plan 1 – 3). Plan 1 is the "Level II Double Tightened" is utilized for the first (b) (4) batches received from a supplier. Plan 2 covers the next (b) (4) receipts from a supplier with a Level II Double Tightened inspection every (b) (4) batch. Plan 3 calls for a Level II Double Tightened inspection every (b) (4) received. Perrigo was sampling (b) (4) Cup (b) (4) under Plan 1 "Level II Double Tightened" as documented on component/Pre-Print Inspection Forms for each of the seven receiving documents reviewed (see **Exhibits 369, 372, 375, 378, 381, 384, and 387**).

Review of each of the SOPs documented above, Physical Defect Criteria #008 (**Exhibits 347/348**), the Perrigo Cup Specification document (**Exhibit 5**) and the component inspection forms completed for each of these receipts finds no documentation that samples were pulled representative of the two (b) (4)) lines. The only documentation of molds numbers pulled (samples) which would also indicate the associated production line based on the diagram in **Exhibit 74** can be found on the back of the Component/Pre-Print Inspection Form (**Exhibits 370, 373, 376, 379, 382, 385, 388**) where the (b) (4) samples are recorded for each incoming component sampling/inspection. However, review of the receiving inspection records associated with vendor lot (b) (4) the information recorded does not appear to document the actual mold numbers inspected. See FDA-483 Item #2 for more regarding this issue.

In addition, the remainder of the AQL sampling performed at the time a shipment is received is not documented as to which mold numbers were sampled and examined for the critical, major and minor defects described in Physical Defect Criteria (b) (4) (**Exhibits 347/348**). As can be seen in the results of the AQL sampling performed for the 7 receipts of vendor batch (b) (4) attached as **Exhibits 370, 373, 376, 379, 382, 385, and 388** zero defects were noted for each of the inspections performed. Cups received under Perrigo Batch #'s (b) (4) (**Exhibits 369/371**) and (b) (4) (**Exhibits 372/374**) were associated with the (b) (4) ((b) (4) (b) (4) (b) (4) (b) (4) and (b) (4) of Children's cough/cold medication being recalled for possibly containing defective dosing cups which are missing the ½ teaspoon dosing line referenced for dosing children ages 2-6.

Discussion with Management:

Regarding this observation, Tami Frederick, Director of Quality Liquid Value Stream pointed out the various quality checks performed by their supplier (b) (4) performed.

OBSERVATION 2

Written procedures for the sampling of packaging and labeling materials are not followed.

SOP (b) (4)) were not followed with regard to selecting (b) (4) different cavity numbers and recording (identifying) which cup (cavity) mold numbers were inspected for Dosing Cup # (b) (4) Examples include:

Supplier Batch #	MFG Date(s)	Perrigo Batch #	Received	Inspected
(b) (4)	7/24-25/07	(b) (4)	7/25/07	7/26/07
"	7/26-27/07	(b) (4)	7/31/07	7/31/07
"	7/31/07	(b) (4)	8/02/07	8/02/07
"	7/27/07	(b) (4)	8/14/07	8/15/07
"	7/27-28/07	(b) (4)	8/14/07	8/15/07
"	7/28-31/07	(b) (4)	8/17/07	8/17/07

Reference: 21 CFR 211.122(a)

Supporting Evidence and Relevance:

Portions of Dosing Cup (b) (4) Supplier batch number (b) (4), was received by Perrigo over a total of (b) (4) shipments. Each receipt was assigned a unique Perrigo Receiving Lot number. The time line prepared for Vendor Batch (b) (4) (**Exhibit 78**) documents the Perrigo Batch number assigned each of these receipts, the quantity of cups received and the actual manufacturing dates represented in the portion of the batch received. This information provided to Perrigo by (b) (4) enabled Perrigo to condense the recall to the first two receipts, both of which contained cups from the first date of production 7/24/07.

As documented in receiving records attached as **Exhibits 369/371** (1st receipt) and **Exhibits 372/374** (2nd receipt) Perrigo would have pulled a total of (b) (4) cup samples for these two receipts.

Section K located on Page 3 of SOP (b) (4) " (**Exhibit 344**) instructs the inspector of Dosage cups that (b) (4) different cavity numbers are to be randomly pulled for testing listed on instruction sheet. That instruction sheet is attached to SOP (b) (4) (**Exhibit 361**) and provides for the listing of the Mold numbers measured. Review of the back page of the Component/pre-Print Inspection Form for (b) (4) reviewed (**Exhibits 370, 376, 379, 382, 385, 388**) finds the inspector simply recorded the numbers (b) (4) in the "List Mold #s" column giving no assurance that the numbers represent the actual mold sample measured.

Discussion with Management:

When pointing out that it appeared the numbers (b) (4) were recorded rather than the actual mold number for the (b) (4) cups for which measurements were checked for the above (b) (4) samples, my observation was met with agreement by the Perrigo representatives present.

REFUSALS

None

GENERAL DISCUSSION WITH MANAGEMENT

At the conclusion of this inspection, FDA-483, Inspectional Observations was issued to Louis W. Yu, Ph.D., Senior Vice President Global Quality & Compliance as I was told he would be the most responsible individual attending the close out meeting. However, Mr. Joseph C. Papa, President & CEO was also in attendance at this meeting. In addition, the following other Perrigo representatives were in attendance:

Greg Kurdys, Sr. VP Operations
Steve Steffes, LVS Manager
John D. Brown, QA-External Operations Director
David Mason, Assistant General Counsel
John T. Hendrickson, Executive VP Global Operations & Supply Chain
Shawn Shirazi, Sr. Director Pre-commercial QA & Technical Affairs
Tami Frederick, Director of Quality, LVS
Kareena Parris, QA Manager
Renee M. Robbins, Director of Quality TVS
Paul Wenenger, VP CHC Global Quality

There were no questions with regard to the written observations presented. Dr. Yu promised a written response within 3-4 weeks.

I pointed out that in addition to the recall follow-up, I reviewed complaints associated with cups packaged with any of their products. In reference to complaint (b) (4) (**Exhibits 52/56**) I warned those present against only investigating complaints pertaining to the quality of the drug and ignoring component-dosage device complaints. I further pointed out that the Center had concerns with dosing cups that contained both TSP and TBSP dose markings which is what caused complaint (b) (4) to be registered.

ADDITIONAL INFORMATION

In response to a request from CDER's Office of Compliance information was collected for 5 (b) (4) and 3 (b) (4) labeled products listed in the 9/4/07 email from Kevin Budich:

1. Attached as **Exhibits 390/396** are the labeling records for (b) (4) brand Sugar Free Tussin Cough (product (b) (4) lot number (b) (4) Exp. 6/08
2. Attached as **Exhibits 397/403** are the labeling records for (b) (4) brand Tussin CF Cough & Cold (product (b) (4) lot number (b) (4) Exp. 6/08
3. Attached as **Exhibits 404/409** are the labeling records for (b) (4) brand Tussin DM Cough Formula (product (b) (4)) lot number (b) (4) Exp. 7/08
4. Attached as **Exhibits 410/415** are the labeling records for (b) (4) brand Children's Pain Relief, Bubble Gum Flavor (product (b) (4)) lot number (b) (4) Exp. 3/08
5. Attached as **Exhibits 416/421** are the labeling records for (b) (4) brand Tussin Cough Formula (product (b) (4)) lot number (b) (4) Exp. 6/08
6. Attached as **Exhibits 422/427** are the labeling records for (b) (4) brand Tussin DM Cough Suppressant Expectorant (product (b) (4)) lot number (b) (4) Exp. 9/08
7. Attached as **Exhibits 428/433** are the labeling records for (b) (4) brand Tussin CF Cough Suppressant Nasal Decongestant Expectorant (product (b) (4) lot # (b) (4) 2 Exp. 9/08
8. Attached as **Exhibits 434/440** are the labeling records for (b) (4) brand Children's Pain Relief Cherry Flavor (product (b) (4)) lot number (b) (4) Exp. 1/09.

As indicated in Exhibits 329/330 and 93/94, each of the above listed products (product numbers) are packaged with dosing cup (b) (4) which bears both teaspoon "TSP" as well as tablespoon "TBSP" dose indication lines.

SAMPLES COLLECTED

As stated previously (b) (4) physical samples were collected for district information only. No analysis necessary. Sample numbers will not be assigned.

VOLUNTARY CORRECTIONS

None

EXHIBITS COLLECTED

1. Specification (drawing) Dosing Cup #(b) (4) in use 3/26/98 – 12/27/00
2. Specification (drawing) Dosing Cup #(b) (4) in use 12/27/00 – present
3-4. Perrigo Cup Specification for Cup #(b) (4) (Rev. A) issued 12/27/00
5. Plastic Cups specification for Part #(b) (4) (Rev G) issued 8/7/06
6. List of Complaints received regarding Dosing Cups
7-14. Complaint PCA(b) (4)
15-22. Complaint PCA(b) (4)
23-31 Complaint(b) (4)
32-35 Complaint(b) (4)
36-42 Complaint(b) (4)
43-47 Complaint(b) (4)
48-51 Complaint(b) (4)
52-56 Complaint(b) (4)
57-59 Process qualification document
60-62 (b) (4) Draft Investigation Report
63-73 (b) (4) Quality Control Document
74 Diagram of dose cup cavity locations on the production line
75-77 Diagrams of dose cups
78 Time line for Dose Cup Vendor Batch(b) (4)
79/82 Dose Cup Volume Verification Protocol(b) (4)
83/92 Volume Verification Testing Results dated 3/27-28/06
93/94 Listing of products that use Cup(b) (4) w/out ½ tsp recommended dosing
95/110 listing of customers, by product number, that utilize Cup(b) (4) & ref. ½ tsp dosing
111/128 Sample product labeling for products using Cup(b) (4) w/out ½ tsp recomm. dosing
129/328 Printout listing all in date marketed lots packaged with Cup(b) (4)
329/330 Listing of products that reference ½ tsp recommended dosing
331/341 Deviation(b) (4) initiated 8/17/09
342/346 SOP(b) (4) ”
347/348 Physical Defect Criteria #(b) (4) ”
349/355 SOP(b) (4)

	(b) (4)
356/362	SOP (b) (4) ”
363/368	SOP (b) (4) ”
369/371	Component/Pre-Print Inspection Form for lot (b) (4)
372/374	Component/Pre-Print Inspection Form for lot (b) (4)
375/377	Component/Pre-Print Inspection Form for lot (b) (4)
378/380	Component/Pre-Print Inspection Form for lot (b) (4)
381/383	Component/Pre-Print Inspection Form for lot (b) (4)
384/386	Component/Pre-Print Inspection Form for lot (b) (4)
387/389	Component/Pre-Print Inspection Form for lot (b) (4)
390/396	Labeling records for (b) (4) Sugar Free Tussin Cough lot (b) (4)
397/403	Labeling records for (b) (4) Tussin CF Cough & Cold lot (b) (4)
404/409	Labeling records for (b) (4) Tussin DM Cough Formula lot (b) (4)
410/415	Labeling records for (b) (4) Children’s Pain Relief lot (b) (4)
416/421	Labeling records for (b) (4) Tussin Cough Formula lot (b) (4)
422/427	Labeling records for (b) (4) DM Cough Suppressant lot (b) (4)
428/433	Labeling records for (b) (4) Tussin CF Cough Suppressant lot (b) (4)
434/440	Labeling records for (b) (4) Children’s Pain Relief lot (b) (4)
441/476	Records related to Batch Number (b) (4)
477/523	Records related to Batch Number (b) (4)
524/534	Records related to Batch Number (b) (4)
535/574	Records related to Batch Number (b) (4)
575/643	Records related to Batch Number (b) (4)
644/663	SOP (b) (4) ”

ATTACHMENTS

#1. August 30, 2007 letter to Sandra Williams, Recall Coordinator, Detroit District
#2. August 30, 2007 letter from Hilde Berberich

Patsy J Domingo, Investigator